

REMARKS

Claims 1-3,6, 15, 22, 24-27,33, 37-39, 42-43, and 45-56 remain pending after amendment.

Interview with Examiner

Applicants thank the Examiner for the courtesy extended toward their representative during the interview of August 12, 2004. During the interview, the outstanding rejection under 35 USC 112 was discussed. No agreement was reached during the interview, with the Examiner indicating that he would defer any decision pending review of applicants' response.

Allowed Claims

Applicants thank the Examiner for the indication of allowability of claims 1-3, 6, 15, 37-39, 42, 43 and 45. However, applicants believe that claims 27, 33 and 56 should also be indicated as being allowable in view of the allowance of those claims depending therefrom and the absence of the citation of any prior art against these claims.

Rejection under 35 USC 112 (paragraph one)

Claims 22-27, 33 and 46-55 stand rejected under 35 USC 112 (paragraph one) as containing subject matter which was not described in the specification in such a way as to

enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner focuses upon the use of the term "prophylaxis" of IBD. This rejection respectfully is traversed.

Initially, as noted above, it is believed that claims 27, 33 and 56 are inadvertently included within the listing of the rejected claims, and should instead be indicated as being allowable.

The specification discloses (page 1, lines 29-38) that IBD covers chronic non-specific inflammatory conditions of the gastro-intestinal tract. It is also disclosed (page 5, lines 11-16) that IBD includes pouchitis. Further, abdominal colectomy with mucosal proctectomy and ileal pouch-anal anastomosis is a preferred treatment for most patients with ulcerative colitis who require surgery. Pouchitis is the most common long term complication of this procedure (page 2, lines 21-25). The cause of pouchitis is unknown but it appears that both the history of ulcerative colitis and increased bacterial concentrations (relative to normal ileum) are factors (page 2, lines 27-30).

Inflammation of the gut mucosa is exacerbated by passage of stool containing bile acids and micro-organisms through the gut. IBD (including pouchitis) is known to go into remission but is also prone to reoccurrence.

Xanthan gum is a high molecular weight polysaccharide gum and is widely used in pharmaceutical compositions as an emulsifying, stabilizing and/or thickening agent (see page 1, lines 11-19). Xanthan gum has been found to be a suitable suspending

vehicle for delivering anti-spasmodics topically along the length of the oseophagus in patients with oseophageal spasm (Evans et al, Pharm. J., 1986, 237:736-737). The gum is accordingly known to have mucoadhesive properties.

Hydroxypropylmethylcellulose (HPMC) is also a polysaccharide and has been used extensively as a suspending agent, tablet excipient, demulcent and/or viscosity increasing agent in pharmaceutical compositions (page 1, lines 21-24). The examples of applicants' specification clearly show that xanthan gum and HPMC can be used to form a gel.

Neither xanthan gum nor HPMC are metabolized by the body. Hence, these compounds pass through the GI tract unchanged. Both polymers are inert (e.g., they are relatively resistant to micro-organisms) and neither undergoes chemical reaction to effect the claimed treatment or prophylaxis of IBD. Instead, both xanthan gum and HPMC contact the gut mucosa and act as a protective layer – e.g., a kind of “dressing” or coating for the interior wall of the gut mucosa. It is disclosed that polysaccharide is placed in contact with the diseased mucosa (page 6, lines 9-13) and that it coats the bowel wall (page 13, lines 10-13). In doing so, the protective layer or shield prevents contact of fecal matter including bowel acids and micro-organisms such as bacteria with the diseased mucosa. By “diseased mucosa” one of ordinary skill in the art will readily appreciate that it is intended to include mucosa that is currently diseased or mucosa which has been diseased.

There are two forms of polysaccharide compositions. In the preferred form, the composition is an enema in which the polysaccharide is a preformed gel (see Examples 1-4). The second form is a delayed release oral form in which the gel is formed in situ following release of the gel-forming components in the gut and contact with intestinal fluid (page 9, line 19 to page 14, line 17 of the specification).

One of ordinary skill in the art would be aware that both xanthan gum and HPMC are polymers that are too large to be absorbed through the gut mucosa. Therefore, xanthan gum and HPMC are not metabolized by the body. The protective layer is not, however, permanent and reapplication of the layer is required for continued treatment or prophylaxis. One of ordinary skill in the art would have appreciated that the shield eventually wears away and passes through the bowel without being absorbed.

Example 4 confirms that, if the enema is applied to an inflamed mucosa in a patient suffering from chronic pouchitis, the indication improves significantly. Similarly, if the composition is applied early enough (prior to the start of inflammation), the protective action of the layer prevents pouchitis from occurring or reoccurring.

Patients with pouchitis (who also have primary sclerosing cholangitis) have a 63% risk of developing chronic pouchitis (Penna C., Dozois, R., Tremaine, W. et al, "Pouchitis after Ileal Pouch-Anal Anastomosis for Ulcerative Colitis Occurs with Increased Frequency in Patients with Associated Primary Sclerosing Cholangitis", *Gut*, 1996, Feb. 38(2),234-239. It would be appropriate to use the enemas of the present

invention as a prophylactic in these cases. In addition, patients with recurrent pouchitis who are brought into remission with antibiotics could be treated with a prophylactic therapy such as these enemas. This has recently been shown to be effective therapy using probiotic therapy for prophylaxis of pouchitis. Minura, T., *Gut*, 53: 108-114, 2004.

In view of the above facts, applicants assert that the claimed method could be successfully practiced with respect to the prophylactic embodiment. One of ordinary skill in the art would readily appreciate and be able to practice the claimed prophylactic method using the recited agents given available information with the requisite degree of predictability, the fact that the amount of direction provided is minimal, the fact that little if any experimentation is required, and the relatively simple nature of the claimed invention.

In view of the above, it is believed that the rejection is without basis and should be withdrawn.

The application is now believed to be in condition for allowance and an early indication of same is earnestly solicited.

In the event that any outstanding matters remain in this application, Applicants request that the Examiner contact James W. Hellwege (Reg. No. 28,808) at (703) 205-8000 to discuss such matters.

Applicant respectfully petitions under the provisions of 37 CFR 1.136(a) and 1.17 for a one-month extension of time in which to respond to the Examiner's Official Action. The Extension of Time fee in the amount of \$110.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Very truly yours,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____


James W. Hellwege
Reg. No. 28,808
P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000